

10/518114

Rec'd PCT/PTO 14 DEC 2004

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
24 December 2003 (24.12.2003)

PCT

(10) International Publication Number
WO 2003/106456 A3

(51) International Patent Classification⁷: **C07D 451/04**, 451/14, A61K 31/46, A61P 3/10, C07D 277/06, 207/06, 207/16, 263/04, 263/06

(74) Agent: SANOFI-SYNTHELABO; c/o György Mihályi and Katalin Mármarosi, Tó u. 1-5, H-1045 Budapest (HU).

(21) International Application Number:
PCT/HU2003/000041

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(22) International Filing Date: 11 June 2003 (11.06.2003)

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
P0202001 14 June 2002 (14.06.2002) HU

Declaration under Rule 4.17:

— of inventorship (Rule 4.17(iv)) for US only

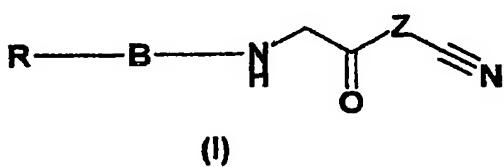
Published:

— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
4 March 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: AZABICYCLO-OCTANE AND NONANE DERIVATIVES WITH DDP-IV INHIBITING ACTIVITY



(57) Abstract: The present invention relates to the novel compounds of the general formula (I) possessing DPP-IV inhibitory activity. These compounds contain tropane (B) building blocks.

WO 2003/106456 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/HU 03/00041

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 7	C07D451/04	C07D451/14	A61K31/46	A61P3/10	C07D277/06
	C07D207/06	C07D207/16	C07D263/04	C07D263/06	

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 19998 A (CIBA GEIGY AG ;VILLHAUER EDWIN BERNARD (US)) 14 May 1998 (1998-05-14) claim 1	1-14
Y	WO 01 34594 A (JACKSON PAUL ;STEINER JOSEPH (US); GUILFORD PHARM INC (US)) 17 May 2001 (2001-05-17) claim 4; examples 44,93	1-14
Y	EP 1 323 710 A (TANABE SEIYAKU CO) 2 July 2003 (2003-07-02) claim 1	1-14
Y	WO 01 96295 A (NOVARTIS ERFIND VERWALT GMBH ;NOVARTIS AG (CH); VILLHAUER EDWIN BE) 20 December 2001 (2001-12-20) claim 1	1-14
	-/-	

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the International filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the International filing date but later than the priority date claimed

- *T* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed Invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed Invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the International search

8 September 2003

Date of mailing of the International search report

13.01.2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Steendijk, M.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/HU 03/0041

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 273 778 A (HADLEY MICHAEL S ET AL) 16 June 1981 (1981-06-16) columns 13-17 -----	1-14
P,Y	WO 03 002553 A (HAFFNER CURT DALE ;MCDOUGALD DARRYL LYNN (US); SMITHKLINE BEECHAM) 9 January 2003 (2003-01-09) claim 20 -----	1-14

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/US 03/00041

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-14

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-14

Compounds of formula I, their preparation and their application as DPP-IV inhibitors

2. claims: 15,16

Intermediates of formulae II and V (R-B-NH₂, R-B-NH-Y)

3. claims: 17-20

Intermediates of formulae VII, VIII, IX and III (proline "Z" analogues)

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 9819998	A	14-05-1998		AU 726186 B2 AU 5318498 A BR 9714130 A CN 1236361 A CZ 9901615 A3 WO 9819998 A2 EP 0937040 A2 HU 0000323 A2 ID 18331 A JP 3217380 B2 JP 2000511559 T KR 2000053081 A NO 992028 A NZ 335146 A PL 332777 A1 RU 2180901 C2 SK 60899 A3 TR 9901004 T2 TW 492957 B ZA 9709985 A		02-11-2000 29-05-1998 29-02-2000 24-11-1999 11-08-1999 14-05-1998 25-08-1999 28-08-2000 26-03-1998 09-10-2001 05-09-2000 25-08-2000 28-04-1999 29-11-1999 11-10-1999 27-03-2002 10-04-2000 21-07-1999 01-07-2002 07-05-1998
WO 0134594	A	17-05-2001		AU 1916401 A CA 2390231 A1 EP 1228061 A1 WO 0134594 A1		06-06-2001 17-05-2001 07-08-2002 17-05-2001
EP 1323710	A	02-07-2003		AU 9419601 A CA 2424964 A1 EP 1323710 A1 AU 9419701 A BR 0114436 A CA 2424600 A1 EP 1325910 A1 WO 0230890 A1 WO 0230891 A1 JP 2002356471 A JP 2002356472 A NO 20031490 A		22-04-2002 18-04-2002 02-07-2003 22-04-2002 01-07-2003 02-04-2003 09-07-2003 18-04-2002 18-04-2002 13-12-2002 13-12-2002 02-06-2003
WO 0196295	A	20-12-2001		AU 1359702 A CA 2411778 A1 WO 0196295 A2 EP 1296974 A2		24-12-2001 20-12-2001 20-12-2001 02-04-2003
US 4273778	A	16-06-1981		AR 225301 A1 AT 24320 T AU 527837 B2 AU 5425579 A AU 543825 B2 AU 9135182 A CA 1218062 A1 CA 1220473 A2 DE 2966476 D1 DE 2967642 D1 DE 2967692 D1 DK 553979 A EP 0013138 A1 EP 0081054 A2		15-03-1982 15-01-1987 24-03-1983 03-07-1980 02-05-1985 10-03-1983 17-02-1987 14-04-1987 12-01-1984 29-01-1987 14-12-1989 15-08-1980 09-07-1980 15-06-1983

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/HU 03/00041

Patent document cited in search report	Publication date		Patent family member(s)	Publication date
US 4273778	A		EP 0220339 A1	06-05-1987
			ES 8101072 A1	01-03-1981
			IE 49737 B1	11-12-1985
			IE 49736 B1	11-12-1985
			JP 1706203 C	27-10-1992
			JP 2072178 A	12-03-1990
			JP 3075548 B	02-12-1991
			JP 55092384 A	12-07-1980
			MX 6255 E	15-02-1985
			NZ 192476 A	14-09-1982
			US 4336259 A	22-06-1982
			US 4544660 A	01-10-1985
			US 4599420 A	08-07-1986
			US 4705858 A	10-11-1987
			ZA 7907054 A	31-12-1980
WO 03002553	A	09-01-2003	WO 03002530 A2	09-01-2003
			WO 03002553 A2	09-01-2003
			WO 03002531 A2	09-01-2003